





What is claimed is:

1	1.	A method of identifying an agent that modulates microtubule	
2	depolymerization, said method comprising the steps of:		
3		(i) contacting a polymerized microtubule with a microtubule severing	
4	protein or a microtub	ule depolymerizing protein in the presence of an ATP or a GTP and said	
5	agent; and	\	
6	-	(ii) detecting the formation of tubulin monomers, dimers or oligomers,	
7	wherein the formation	n of said tubulin monomers, dimers, or oligomers indicates that said	
8	agent modulates micr	otubule depolymerization	
1	2.	The method of claim 1, wherein said polymerized microtubule is	
2	labeled with DAPI.		
1	3.	The method of claim 1, wherein said detecting is by fluorescent	
2	resonance energy tran	nsfer (FRET).	
1	4.	The method of claim 2, wherein said detecting comprising detecting a	
2		ce of said labeled microtubule.	
	5	as of one subside microtabalo.	
1	5.	The method of claim 1, wherein said detecting comprises centrifuging	
2	said tubulin monome	rs if present.	
1	6.	The method of claim 1, wherein said microtubules are stabilized by	
2	contact with an agent	selected from the group consisting of paclitaxel, a paclitaxel analogue,	
3	and a non-hydrolyzat	ole nucleotide GTP analogue.	
1	7	The most of a falling 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
2	7. surface.	The method of claim 1, wherein said microtubule is attached to a solid	
2	surface.		
1	8.	The method of claim 7, wherein said microtubule is attached to said	
2	surface by binding w	ith an agent selected from the group consisting of an inactivited	
3	microtubule motor protein, an avidin-biotin linkage, an anti-tubulin antibody, a microtubule		
4	binding protein (MAP), and a polylysine		

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1	9.	The method of claim	1, wherein said a microtubule severing protein or
2	a microtubule depoly	merizing protein is sel	ected from the group consisting of a katanin, a
3	p60 subunit of a kata	nin, an XKCM1, and a	OP18 polypeptide.

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- 1 10. The method of claim 9, wherein said microtubule severing protein is a 2 katanin or a p60 subunit of a katanin.
- 1 11. The method of claim 10, wherein said p60 subunit of a katanin is a polypeptide of claim 26.
- 1 12. The method of claim 10, wherein said p60 subunit is a polypeptide 2 having the amino acid sequence of SEQ ID NO: 1.
- 1 13. The method of claim 1, wherein said method is performed in an array where said array comprises a multiplicity of reaction mixtures. each reaction mixture comprising a distinct and distinguishable domain of said array, and wherein said steps are performed in each reaction mixture.
- 1 14. The method of claim 13, wherein said array comprises a microtitre 2 plate.
 - 15. The method of claim 13, wherein said array comprises at least 48 of said reaction mixtures.
- 1 16. The method of claim 13, wherein said agent is one of a plurality of agents and wherein each reaction mixture comprises one agent of said plurality of agents.
- 1 A method of identifying a the apeutic lead compound that modulates 2 depolymerization or severing of a microtubule system, said method comprising the steps of:
- i) providing an assay mixture comprising a katanin p60 subunit and a

4 microtubules;

- 5 ii) contacting said assay mixture with a test compound to be screened
- for the ability to inhibit or enhance the microtubule sevening or ATPase activity of said p60
- 7 subunit; and
- 8 iii) detecting specific binding of said test compound to said p60
- 9 subunit or a change in the ATPase activity of said p60 subuhit.



substitutions.

1	18. The method of claim 17, wherein said detecting comprises detecting			
2	ATPase activity utilizes malachite green as a detection reagent.			
1	19. The method of claim 17, wherein said p60 subunit is labeled and said			
2	test agent is attached to a solid support.			
1	20. The method of claim 17, wherein said test agent is labeled and said p60			
2	subunit is attached to a solid support.			
1	21. The method of claim 17, wherein said microtubules are stabilized by			
2	contact with an agent selected from the group consisting of paclitaxel, a paclitaxel analogue,			
3	and a non-hydrolyzable nucleotide GTP analogue			
1	22. The method of claim 17, wherein said method is performed in an array			
2	where said array comprises a multiplicity of reaction mixtures. each reaction mixture			
3	comprising a distinct and distinguishable domain of said array, and wherein said steps are			
4	performed in each reaction mixture.			
1	23. The method of claim 22, wherein said array comprises a microtitre			
2	plate.			
1	24. The method of claim 22, wherein said array comprises at least 48 of			
2	said reaction mixtures.			
1	25. The method of claim 22, wherein said agent one of a plurality of agents			
2	and wherein each reaction mixture comprises one agent of said plurality of agents			
1	26. A polypeptide having microtubule severing activity, said polypeptide			
2	comprising an isolated p60 subunit of a katanin, wherein said p60 subunit is encoded by a			
3	nucleic acid that hybridizes under stringent conditions with a nucleic acid that encodes the			
4	amino acid SEQ ID NO: 1.			
1	27. The polypeptide of claim 26. wherein said polypeptide is the			
2	polypeptide of SEQ ID NO: 1 or the polypeptide of SEQ ID NO: 1 having conservative			

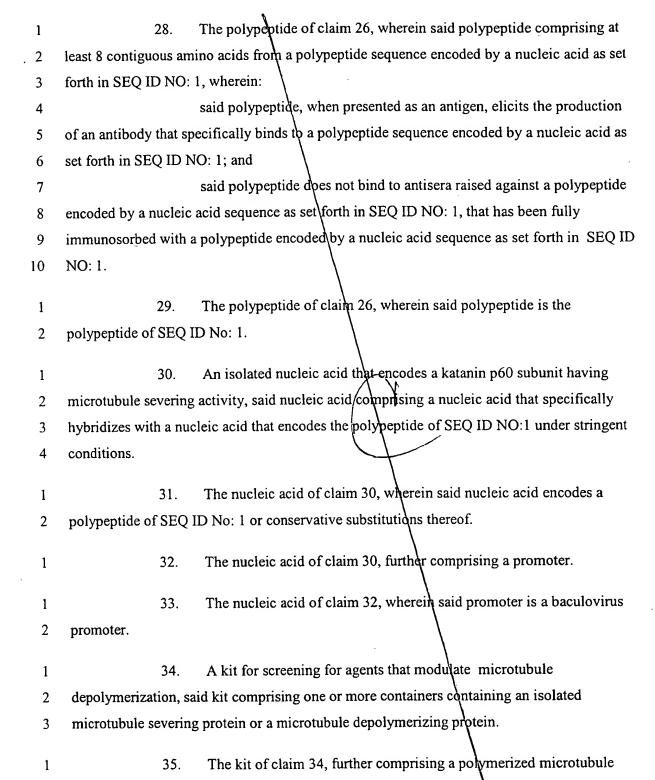
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labeled with DAPI.

36.

with paclitaxel or a paclitaxel derivative.



The kit of claim 34, wherein said microtubule is stabilized by contact

a microtubule.

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1	37. The kit of claim 36, wherein said microtubule is attached to a solid
. 2	surface.
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	38. The kit of claim 37, wherein said microtubule is attached to said
2	surface by binding with a motor protein.
1	39. The kit of claim 34, wherein said microtubule severing protein or
2	microtubule depolymerizing protein is selected from the group consisting of a katanin, a p60
3	subunit of a katanin, an XKCM1, and a OP 8 polypertide.
1	40. The kit of claim 39, wherein said microtubule severing protein is a
2	katanin or a p60 subunit of a katanin.
1	41. The kit of claim 34, wherein said p60 subunit of a katanin is a
2	polypeptide of claim 26.
1	42. The kit of claim 34, wherein said microtubule severing protein or
2	microtubule depolymerizing protein is attached to a solid surface.
1	43. A method of screening for an agent that alters microtubule
2	polymerization or depolymerization or severing, said method comprising:
3	providing labeled tubulin;
4	contacting said labeled tubulin with said agent to produce contacted
5	tubulin;
6	comparing the fluorescence intensity or pattern of said contacted
7.	tubulin with the fluorescence intensity or pattern of labeled tubulin that is not contacted with
8	said agent wherein a difference in fluorescence pattern or intensity between the contacted and
9	the not contacted tubulin indicates that said agent alters microtubule polymerization or
10	depolymerization.
1	44. The method of claim 43, wherein said labeled tubulin is in the form of
2	tubulin monomers, tubulin dimers, or tubulin oligomers.
1	45. The method of claim 43, wherein said labeled tubulin is in the form of

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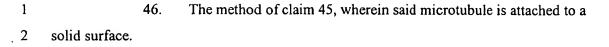
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- 1 47. The method of claim 45, Wherein said label is selected from the group 2 consisting of DAPI, ANS, Bis-ANS, ruthenium red, cresol violet, and DCVJ.
 - The method of claim 47, wherein said label is DAPI. 48.
- 49. The method of claim 46, wherein said microtubule is attached to said 1 2 surface by binding with an agent selected from the group consisting of an inactivated microtubule motor protein, an avidin-biotin linkage, an anti-tubulin antibody, a microtubule 3 4 binding protein (MAP), a polyarginine, a polyhistidine, and a polylysine.
- The method of claim 43\ wherein said contacting further comprises 1 50. 2 contacting said tubulin with a microtubule depdlymerizing protein or a microtubule severing 3 protein.
- The method of claim 50, wherein said a microtubule severing protein 51. 1 2 or a microtubule depolymerizing protein is selected from the group consisting of a katanin, a 3 p60 subunit of a katanin, an XKCM1, and a OP18 polypeptide.
 - 52. The method of claim 51, wherein said microtubule severing protein is a katanin or a p60 subunit of a katanin.
- 1 53. The method of claim 52, wherein said p60 subunit of a katanin is a 2 polypeptide of claim 26.
- 1 54. The method of claim 52, wherein said p60 subunit is a polypeptide 2 having the amino acid sequence of SEQ ID NO: 1.
 - The method of claim 43, wherein said method is performed in an array 55. where said array comprises a multiplicity of reaction mixtures. each reaction mixture comprising a distinct and distinguishable domain of said array, and wherein said steps are performed in each reaction mixture.
- 1 56. The method of claim 55, wherein said array comprises a microtitre 2 plate.







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57. The method of claim 55, wherein said array comprises at least 48 of 1 2 said reaction mixtures.

- The method of daim 55, wherein said agent one of a plurality of agents 58. and wherein each reaction mixture comprises one agent of said plurality of agents.
- The method of claim 43, further comprising listing the agents that 1 59. 2 alters microtubule polymerization, depolymerization, or severing into a database of therapeutic lead compounds that act on the dytoskeletal system.. 3